REMARKS

Claims 1-10 are allowed. Claims 13-15 have been rejected. Reconsideration of the rejection is respectfully requested in view of the above amendments and the following remarks.

Claim Amendments

Method of treatment claims 13 and 14 have been cancelled, without prejudice or waiver of applicant's right to pursue the subject matter thereof in one or more continuing applications. Claim 15 has been amended to more specifically direct it to a method for inhibiting the production or effect of TNFα (rather than TNF and IL-1, as originally claimed) in response to the Examiner's enablement rejection, as detailed further below. New claim 16 has been added, directed toward the treatment of rheumatoid arthritis, which the Examiner acknowledges is enabled.

Inasmuch as these amendments are directly responsive to and consistent with the Examiner's comments in the Final Action, do not require any further search, and are believed to place this application in condition for allowance, entry of these amendments after Final is believed to be appropriate and is respectfully requested.

Status of the Claims

Following entry of the above amendments, claims 1-10 have been allowed, claims 11-14 have been cancelled, and claim 15 stands rejected (see discussion below). Claim 16 is newly presented herein at the Examiner's suggestion as being enabled, and therefore claim 16 is understood to also be in condition for allowance.

Claim Rejections – 35 U.S.C. § 112

Method claims 13-15 have been rejected under 35 U.S.C. § 112, first paragraph. The section 112, first paragraph rejection begins at page 2 of the Action, the beginning portion of which is quoted below (with added emphasis) for ease of reference wit respect to the argument which follow::

> Claims 13-15 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating rheumatoid arthritis, does not reasonably provide enablement for treating any or all disease or conditions mediated by the production or effect of p38 kinase, TNF-α, or IL-1 including those yet to be discovered as due to p38 kinase, TNF-α or IL-1 i generically embraced in the claim language. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. Following reasons apply.
>
> The instant claims 13-15 are drawn to "treating a disease or medical conditions mediated by the production or effect of p38 kinase, TNF-α, or IL-1". The scope of the claims includes not only any or all diseases/conditions but also those diseases/condition yet to be discovered as due to by the production or effect of p38 kinase, TNF-α, or IL-1 for which there is no enabling disclosure. In addition, the scope of these claims includes treatment of various diseases, which is not adequately enabled solely based in the production or effect of p38 kinase, TNF-α, or IL-1 activity of the compounds provided in the specification, pages, 1-3 and 39-43. The instant compounds are disclosed to have ability to reduce by the production or effect of p38 kinase, TNF-α, or IL-1 and it is recited that the instant compounds are therefore useful in treating any or all disease where such production or effect of p38 kinase, TNF-α, or IL-1 activity is implicated, for which applicants provide no competent evidence. Furthermore, the applicants have not provided any competent evidence that the instantly disclosed tests are highly predictive for all the uses disclosed and embraced by the claim language for the intended host. Moreover many if not most of neurodegenerative diseases such as Alzheimer's disease, multiple sclerosis, and AIDS etc. are very difficult to treat and at present there is no known drug, which can successfully reverse the course of these diseases, despite the fact that there are many drugs, which can be used for "inflammatory condition". That a single class of compounds can be used to treat all diseases embraced in the claims is an incredible finding for which applicants have not provided supporting evidence.

> Note substantiation of utility and its scope is required when utility is "speculative", "sufficiently unusual" or not provided. See Ex parte Jovanovics, 211 USPQ 907, 909; In re Langer 183 USPQ 288. Also note Hoffman v. Klaus 9 USPQ 2d 1657 and Ex parte Powers 220 USPQ 925 regarding type of testing needed to support in vivo uses. Next, applicant's attention is drawn to the Revised Interim Utility and Written Description Guidelines, at 64 FR 71427 and 71440 (December 21, 1999) wherein it is emphasized that 'a claimed invention must have a specific and substantial utility'. The disclosure in the instant case is not sufficient to enable the instantly claimed method treating solely based on the activity disclosed for the compounds. . . ."

(Action at pages 2-4; emphasis added with regard to certain points specifically discussed below). The Action continues on pages 4 through 6 to recite various factors for evaluating enablement. It is noted that the Examiner again characterizes "the nature of the invention" as being "[t]herapeutic use of the compounds in treating diseases that are mediated by production or effect of p38 kinase, TNF-α, or IL-1 activity." (Action at page 4, emphasis added).

The rejection is respectfully traversed in view of the above amendments and the reasons set forth below.

In order to expedite the allowance of this application, claims 13 and 14 (to which the section 112 rejection actually seems to be directed) have been cancelled, without prejudice. New claim 16 is directed toward the treatment of rheumatoid arthritis, which the Examiner acknowledges is enabled, at page 2 of the Action.

While the cancellation of claims 13 and 14 renders their rejection moot, Applicant wishes to make very clear that the cancellation of these claims does not constitute acquiescence or agreement with the stated grounds and reasoning for their rejection. Claims 13 and 14, as the Examiner states, are directed toward "a method of treating a disease or medical condition mediated by the production or effect" of "p38 kinase" or the production or

effect of "TNF or IL-1," respectively, which scope and format is used as the basis for the rejection. However, claim 15 is not directed toward a method of "treating a disease or medical condition mediated by the production or effect" of p38 kinase, TNF-α, or IL-1 activity, and it therefore is not clear on what basis claim 15 has been rejected. Rather, claim 15 provides:

> 15. A method for inhibiting the production or effect of TNFα in a warm-blooded animal in need thereof comprising administering to said animal a TNFα inhibiting amount of a pyrimidine compound of the Formula I, or a pharmaceutically-acceptable salt or in-vivo-cleavable ester formed from an available carboxy group thereof, as defined in claim 1.

Thus, claim 15 is directed toward the production of a pharmacological effect (inhibiting the production or effect of TNFα) by administration of a compound as specifically claimed in allowed claim 1. Thus, as a starting point, there can be no question regarding the utility and enablement of compounds of claim 1.

Moreover, there can be no question regarding the utility of claim 15. At pages 3-4 of the Action, the Examiner asserts "that a single class of compounds can be used to treat all diseases embraced in the claims is an incredible finding for which applicants have not provided supporting evidence," noting that "substantiation of utility and its scope is required when utility is 'speculative', 'sufficiently unusual' or not provided." Examiner then cites the "Interim Utility and Written Description Guidelines" (December 21, 1999) as requiring that a claimed invention must have a specific and substantial utility. It is respectfully noted that the Examiner appears to be intermixing the utility and enablement guidelines. In any event, the Utility Guidelines relied upon by the Examiner (now incorporated in the MPEP as Section 2107) make very clear that an applicant need only identify a single specific and substantial utility:

> It is common and sensible for an applicant to identify several specific utilities for an invention, particularly where the invention is a product (e.g., a machine, an article of manufacture or a composition of matter). However, regardless of the category of invention that is claimed (e.g., product or process), an applicant need only make one credible assertion of specific utility for the claimed invention to satisfy **35 U.S.C. 101** and **35 U.S.C. 112**; additional statements of utility, even if not "credible," do not render the claimed invention lacking in utility. See, e.g., *Raytheon v. Roper*, 724 F.2d 951, 958, 220 USPQ 592, 598 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 835 (1984) ("When a properly claimed invention meets at least one stated objective, utility under **35 U.S.C. 101** is clearly shown."); *In re Gottlieb*, 328 F.2d 1016, 1019, 140 USPQ 665, 668 (CCPA 1964) ("Having found that the antibiotic is useful for some purpose, it becomes unnecessary to decide whether it is in fact useful for the other purposes 'indicated' in the specification as possibly useful."); *In re Malachowski*, 530 F.2d 1402, 189 USPQ 432 (CCPA 1976); *Hoffman v. Klaus*, 9 USPQ2d 1657 (Bd. Pat. App. & Inter. 1988). Thus, if applicant makes one credible assertion of utility, utility for the claimed invention as a whole is established.

(MPEP § 2107.02 I., Rev. 1, Feb. 2003 at 2100-37).

Claim 15 is directed toward a method for inhibiting the production or effect of TNFα in a warm-blooded animal. The specification clearly asserts and establishes that the claimed method is effective for the treatment of rheumatoid arthritis, which is a specific, substantial and credible utility, as the Examiner necessarily has recognized by acknowledging that a method of treating rheumatoid arthritis is enabled.

Moreover, the Federal Circuit has held that a pharmacological activity as claimed in claim 15, in and of itself is sufficient to meet the utility requirement:

> Courts have repeatedly found that the mere identification of a pharmacological activity of a compound that is relevant to an asserted pharmacological use provides an "immediate benefit to the public" and thus satisfies the utility requirement. As the Court of Customs and Patent Appeals held in *Nelson v. Bowler*:
>
> > Knowledge of the pharmacological activity of any compound is obviously beneficial to the public. It is

> inherently faster and easier to combat illnesses and alleviate symptoms when the medical profession is armed with an arsenal of chemicals having known pharmacological activities. Since it is crucial to provide researchers with an incentive to disclose pharmacological activities in as many compounds as possible, we conclude that adequate proof of any such activity constitutes a showing of practical utility.

(MPEP § 2107.01, citing *Nelson v. Bowler*, 626 F.2d 853, 856, 206 USPQ 881, 883 (CCPA 1980); MPEP Rev. 1, Feb. 2003).

It is therefore respectfully submitted that claim 15 meets the utility requirement as set forth and interpreted by the relevant decisions of the Court of Appeals for the Federal Circuit, as summarized and restated in the guidelines incorporated in the MPEP. Accordingly, the Examiner statements in the paragraph bridging pages 2 and 3 of the Action with respect to utility are inconsistent with the applicable law, and do not provide support to the rejection.

At pages 4-6 of the Action, the Examiner discusses the factors to be considered in evaluating enablement, derived from *In re Wands*, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). More precisely, the *Wands* factors are directed to evaluating whether or not "*undue experimentation*" would be required to practice the invention *as claimed.* The relevant factors that may be considered "include" those taken from the case law and set forth in MPEP 2164.01(a). However, the underlying determination is whether undue experimentation would have been required to carry out the invention as claimed.

The starting point in any such analysis is, necessarily, the breadth of the claims. As noted above, claim 15 does not claim the treatment of diseases, but rather is directed toward "inhibiting the production or effect of TNFα" in a warm blooded animal, by administration of a TNFα inhibiting amount of a compound as claimed in claim 1. As discussed above, the

utility requirement is met by the disclosure and acknowledged enablement of the method for treating rheumatoid arthritis. Whether or not inhibiting the production or effect of TNFα may also be effective in the treatment of other diseases is immaterial to utility (see MPEP § 2107.02 I. discussed above). For purposes of enablement, however, the breadth of claim 15 is inhibiting the production or effect of TNFα by administration of a compound of claim 1, which, as discussed further below, is expressly demonstrated in the specification.

Given this breadth of claim 15, the question is then whether the guidance provided by the specification, considered in context of the art as a whole, enables one to practice this invention as claimed without undue experimentation. There is no question but that one is enabled to make the compounds needed to practice the invention, as evidenced by the allowance of compound claim 1. Clear guidance on how to carry out the claimed method is provided by the assays detailed in the specification beginning at page 40. These assays include:

- *In vitro* cell-based assays including the PBMC assay at page 40 (ability of the compounds to inhibit TNFα production using human peripheral blood mononuclear cells which synthesize and secrete TNFα when stimulated with lipopolysaccharide); and the Human Whole Blood assay at page 41 (ability of the compounds to inhibit TNFα production in human whole blood); and
- The test of the compounds as an anti-arthritic agent at page 42, including literature support at page 43.

It is therefore submitted that with this guidance, persons skilled in the art would be able to practice *the invention that is claimed in claim 15* without undue experimentation. Therefore, the invention that as actually claimed in claim 15 is enabled by the specification,

particularly as claim 15 has been amended above. Accordingly, it is respectfully requested that the rejection of claim 15 be withdrawn, and that this claim be allowed.

Conclusion

In view of the above amendments and the foregoing argument, it is believed that all claims now pending in this application are in condition for allowance, and a notice to that effect is respectfully requested. If, however, the Examiner is of the view that any ground for rejection should be continued, it is respectfully requested that the Examiner telephone the undersigned at the telephone number given below, so that a quick and appropriate resolution of any outstanding issue can be obtained.

EXCEPT for issue fees payable under 37 C.F.R. § 1.18, the Director is hereby authorized by this paper to charge any additional fees during the entire pendency of this application including fees due under 37 C.F.R. §§ 1.16 and 1.17 which may be required, including any required extension of time fees, or credit any overpayment to Deposit Account 50-0310. This paragraph is intended to be a **CONSTRUCTIVE PETITION FOR EXTENSION OF TIME** in accordance with 37 C.F.R. § 1.136(a)(3).

Respectfully Submitted,
Morgan Lewis & Bockius LLP

Date: April 28, 2004 By: _____
Donald J. Bird
Registration No. 25,323
Tel. No.: (202) 739-5320
Fax No.: (202) 739-3001

Morgan Lewis & Bockius LLP
Customer No. **09629**
1111 Pennsylvania Avenue, N.W.
Washington, D.C. 20004
Tel. No.: 202-739-3000
DJB:mk